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C9
cont
receptor 1, complement receptor 2, decay accelerating factor,
membrane cofactor protein, C4 binding protein, and factor H.

Remarks

Objections and Rejections under 37 C.F.R. §112

The specification has been objected to on the basis that the amended reference to Figure 2 on page 14 does not correspond to the drawing. The references to "labeled" have now been deleted; these are unnecessary. The only sequence shown in Figure 2A and 2B is for CR1; the reference to corresponding regions in DAF and MCP is to define how one would determine the homologous regions and conserved amino acid sequence. The actual amino acid sequences of all three proteins are in the public domain.

The sequences cited in the specification for CR1, CR2, DAF, and MCP, referenced at pages 16 and 17, and incorporated by reference, have been inserted into the specification as requested by the Examiner.

All pending claims have been rejected under 35 U.S.C. §112 as indefinite and non-enabled.

The spelling of "consensus" has been corrected in claims 1 and 16. The careful review of the examiner is appreciated.

Claims 1, 16, and 34 have been amended to remove the language relating to substitutions and refer instead solely to

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proteins have repeats of short consensus regions, rearranged short consensus regions, or which are truncated to retain as few as three short consensus regions. Claims 6, 7, 21, and 22 have been cancelled.

Claim 14 has been amended to delete the "essentially of" language.

The objected to language "defined" has been deleted from claims 1 and 16. Claims 1 and 16 have been amended to provide antecedent basis for "the complement regulatory activity" and "decay accelerating activity".

The withdrawal of the prior art rejections is greatly appreciated.

Examination and reconsideration of all claims 1-5, 8-20, 23-32 and 34, as amended, is earnestly solicited. All claims as currently pending are attached in an appendix for the convenience of the Examiner.

Respectfully submitted,



Patrea L. Pabst
Reg. No. 31,284

Date: November 15, 1995
Arnall Golden & Gregory
2800 One Atlantic Center
Atlanta, GA 30309-3450
(404) 873-8794

Appendix: Claims as currently pending

1. (twice amended) An analog of a protein regulating complement activation having short consensus repeats of amino acid sequence selected from the group complement regulating proteins consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H, and those complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, wherein said protein analog is selected from the group consisting of complement regulating [proteins] protein analogs containing short consensus repeats derived from a second, different complement regulating protein, complement regulating [proteins] protein analogs wherein the short consensus repeats are rearranged[, complement regulating proteins having defined amino acid substitutions in the short consensus repeats selected from the group consisting of repeats having binding activity, cofactor activity, and decay accelerating activity, wherein the substitution alters the activity of the naturally occurring complement regulatory protein], and complement regulating [proteins] protein analogs consisting of as few as three short [consenses] consensus repeats, wherein the protein analog binds C3b, C4b or C3b and C4b.

2. (amended) The analog of claim 1 wherein the complement regulatory protein analog has an activity [is] selected from the group consisting of C3b binding activity, C3b cofactor activity, C4b binding activity, C4b cofactor activity, and decay accelerating activity.

3. The analog of claim 2 wherein the protein is complement receptor one.

4. The analog of claim 2 wherein the protein is decay accelerating factor.

5. The analog of claim 2 wherein the protein is factor Please cancel claims 6 and 7.

8. (amended) The analog of claim 2 wherein the protein contains a change within a short consensus repeat that corresponds with a change to complement receptor one as shown in Sequence ID No. 2 selected from the group consisting of:

CR1-4 with its first 122 amino acids (SCR1-2) replaced with CR1 amino acids 497-618 (SCR 8-9) and CR1-4(8,9) with deletion of 194-253; substitution of amino acids 271-543 with: T-R-T-T-F-H-L-G-R-K-C-S-T-A-V-S-P-A-T-T-S-E-G-L-R-L-C-A-A-H-P-R-E-T-G-A-L-Q-P-P-H-V-K, or structurally similar amino acids.

9. (amended) The analog of claim 2 wherein the protein contains a change within a short consensus repeat that corresponds with a change to complement receptor one as shown in Sequence ID No. 2 selected from the group consisting of:

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79: D; 37,39: Y,D; 92: T; 109-112: N-A-A-H; 109-112, 114-117, 121: N-A-A-H, S-T-K-P...Q; 114-117, 121: N-A-A-H, S-T-K-P...Q; 116: K; 116,117: K-P; 92-94: K...Y; 99,103,106: S...T...I; 109-112: P-T-V-I; 110: T; 111: V; 112: I; 114: D; 115: N; 121: D; 117: T; 1,3: Q...N; 6-9: E-W-L-P; 12-16, 18-21: K-L-K-T-Q...N-A-S-D; 27,29: S...K; 37: S; 44, 47, 49: I...K...S; 52-54, 57, 59: T-G-A...R...R; 78-79, 82: K-G...F; 85, 87: Q...K; 12-16, 18-21: R-P-T-N-L...D-E-R-E; 27,29: Y...N; 35, 64-65, 94: G...R-N...Y, substitutions with structurally similar amino acids, and combinations thereof.

10. (amended) The analog of claim 2 wherein the complement regulatory protein is decay accelerating factor wherein one or more substitutions are introduced into the region of the protein corresponding to decay accelerating factor short consensus repeats SCRs 2-3 as shown in Sequence ID No. 6 selected from the group consisting of 180-187: S-T-K-P-P-I-C-Q; 175-178: N-A-A-H; 175-187: S-T-K-P-P-I-C-Q-N-A-A-H; 130: R; 145: D; 77-84: K-L-K-T-Q-T-N-A-S-D; 90-92: S-L-K, substitutions with structurally similar amino acids, and combinations thereof.

11. The analog of claim 1 wherein the complement regulatory protein is factor H comprising sequences conferring on the protein an activity selected from the group consisting of C3b binding activity, C3b cofactor activity, C4b binding activity, and C4b cofactor activity, wherein the sequences are derived from a protein selected from the group consisting of complement receptor 1, membrane cofactor protein, C4 binding protein, and factor H..

12. The analog of claim 1 comprising at least one short consensus repeat derived from a different protein selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H.

13. (amended) The analog of claim 1 wherein the protein has C3b cofactor activity, C4b cofactor activity and decay accelerating activity.

14. (amended) The analog of claim 1 wherein the region of the protein having biological activity consists [essentially] of three short consensus regions and has two complement regulatory activities.

15. The analog of claim 1 further comprising a pharmaceutically acceptable carrier for administration to a patient in need thereof.

16. (twice amended) A method for making an analog of a protein regulating complement activation having short consensus repeats of amino acid sequence selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding

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protein, and factor H, and these complement regulating proteins wherein the carboxy terminus is removed to allow the protein to be secreted, comprising

constructing a DNA sequence encoding a protein analog selected from the group consisting of complement regulating [proteins] protein analogs containing short consensus repeats derived from a second, different complement regulating protein, complement regulating [proteins] protein analogs wherein the short consensus repeats are rearranged[, complement regulating proteins having defined amino acid substitutions in the short consensus repeats selected from the group consisting of repeats having binding activity, cofactor activity, and decay accelerating activity, wherein the substitution alters the activity of the naturally occurring complement regulatory protein], and complement regulating [proteins] protein analogs consisting of as few as three short [consenses] consensus repeats, wherein the protein analog binds C3b, C4b, or C3b and C4b, and

expressing the DNA sequence in a suitable host for expression of the protein.

17. (amended) The method of claim 16 wherein the complement regulatory protein analog has an activity [is] selected from the group consisting of C3b binding activity, C3b cofactor activity, C4b binding activity, C4b cofactor activity, and decay accelerating activity.

18. The method of claim 16 wherein the protein is complement receptor one.

19. The method of claim 16 wherein the protein is decay accelerating factor.

20. The method of claim 16 wherein the protein is factor H.

Please cancel claims 21 and 22.

23. (amended) The method of claim 17 wherein the protein analog contains a change within a short consensus repeat that corresponds with a change to complement receptor one as shown in Sequence ID No 2 selected from the group consisting of:

CR1-4 with its first 122 amino acids (SCR1-2) replaced with CR1 amino acids 497-618 (SCR 8-9) and CR1-4(8,9) with deletion of 194-253; substitution of amino acids 271-543 with: T-R-T-T-F-H-L-G-R-K-C-S-T-A-V-S-P-A-T-T-S-E-G-L-R-L-C-A-A-H-P-R-E-T-G-A-L-Q-P-P-H-V-K, or structurally similar amino acids.

24. (amended) The method of claim 17 wherein the protein analog contains a change within a short consensus repeat that corresponds with a change to complement receptor one as shown in Sequence ID No. 2 selected from the group consisting of: 79: D; 37,39: Y,D; 92: T; 109-112: N-A-A-H; 109-112, 114-117, 121: N-A-A-H, S-T-K-P...Q; 114-117, 121: N-A-A-H, S-T-K-P...Q;

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116: K; 116,117: K-P; 92-94: K...Y; 99,103,106: S...T...I; 109-
112: P-T-V-I; 110: T; 111: V; 112: I; 114: D; 115: N; 121: D;
117: T; 1,3: Q...N; 6-9: E-W-L-P; 12-16, 18-21: K-L-K-T-Q...N-A-
S-D; 27,29: S...K; 37: S; 44, 47, 49: I...K...S; 52-54, 57, 59:
T-G-A...R...R; 78-79, 82: K-G...F; 85, 87: Q...K; 12-16, 18-21:
R-P-T-N-L...D-E-R-E; 27,29: Y...N; 35, 64-65, 94: G...R-N...Y,
substitutions with structurally similar amino acids, and
combinations thereof.

25. (amended) The method of claim 17 wherein the complement regulatory protein is decay accelerating factor wherein one or more substitutions are introduced into the region of the protein corresponding to decay accelerating factor short consensus repeats SCRs 2-3 as shown in Sequence ID No. 6 selected from the group consisting of 180-187: S-T-K-P-P-I-C-Q; 175-178: N-A-A-H; 175-187: S-T-K-P-P-I-C-Q-N-A-A-H; 130: R; 145: D; 77-84: K-L-K-T-Q-T-N-A-S-D; 90-92: S-L-K, substitutions with structurally similar amino acids, and combinations thereof.

26. The method of claim 16 wherein the complement regulatory protein is factor H comprising sequences conferring on the protein an activity selected from the group consisting of C3b binding activity, C3b cofactor activity, C4b binding activity, and C4b cofactor activity, wherein the sequences are derived from a protein selected from the group consisting of complement receptor 1, membrane cofactor protein, C4 binding protein, and factor H.

27. (amended) The method of claim 16 comprising inserting into the protein analog at least one short consensus repeat derived from a different protein selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H.

28. (amended) The method of claim 16 wherein the protein has C3b cofactor activity, C4b cofactor activity and decay accelerating activity.

31. (amended) A DNA sequence which encodes an analog of claim 1.

32. (amended) The DNA sequence of claim 31 inserted into an expression vector operably linked to control sequences compatible with a compatible host which is capable, when transformed into the host cell, of expressing a DNA encoding an analog of claim 1.

34. (twice amended) A method for enhancing the C4b or C3b cofactor activity of a complement regulatory protein, wherein the protein has either C3b or C4b cofactor activity, comprising adding sequences to the protein conferring binding of the other ligand, either C4b or C3b, wherein the sequences are present in a protein selected from the group of naturally occurring complement

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